REMARKS

Claims 14 and 67-84 are pending and are the subject of the present office action finally rejecting the claims.

Priority

Applicants note that in the previous office action the Examiner made certain assertions regarding the instant application's benefit of priority. Applicants do not agree with the Examiner's assertions regarding the effective filing date of the claims presented in this application, and expressly reserve the right to dispute such assertions if necessary at a later time. Applicants also believe that the response provided herein fully addresses the outstanding rejections in a manner that does not require resolution of the question of priority of Applicants' claims.

Section 102(e) Rejections

Claims 14 and 67-83 were rejected under Section 102(e) as being anticipated by Emery et al., US Patent 5,885,800. Applicants respectfully traverse this rejection. As indicated in Applicants' previously filed response and as discussed further below, it is Applicants' position that the Emery et al. patent cannot properly be applied as "prior art" under Section 102(e) against the claims presented in the instant application.

The Emery et al. patent clearly does not meet the requirements of utility OR enablement, and Applicants respectfully submit that if the Emery et al. specification were examined pursuant to the current

guidelines under Section 101 and 112, it likely would never have issued as a patent.[1] The Examiner asserts that pursuant to MPEP Section 2122 and *In re Schoenwald*, a reference need not disclose utility in order for it to be anticipatory art. The Examiner, however, does not refer to or establish why Emery et al. satisfies the requirements of Section 112. Applicants note that it is well-settled law that a patent shall have effect under 35 U.S.C. § 102(e) as of a particular date only to the extent that there is a sufficient disclosure under 35 U.S.C. § 112, first paragraph, for the subject matter in question. The Examiner is referred to In re Wertheim, 646 F2d 527, 209 USPQ 554 (CCPA 1981), as well as MPEP 2136.03, sub-heading IV, which provide that the claims of a reference patent must be supported in the manner required by 35 USC 112 in the priority application whose date is relied on to establish the prior art status of the patent. The disclosure of such an application must include a use that supports the claims under Section 112. If it does not, that application is simply not available as part of the prior art.

Although Emery et al. disclose certain sequence structure information for the molecule they refer to as "TR4", the patent merely speculates what the function or activity TR4 might be. The disclosure in Emery et al. relating to what TR4 may be used for or how it may be used is entirely prophetic. In other words, the disclosure of Emery et al. represents nothing more than a "paper" proposal for future research and is not an enabling disclosure for the skilled artisan. The Examiner asserts that an "actual reduction to practice is not required for this to be an anticipatory reference." (Office action at page 3, lines 16-17). As discussed above, though, the relevant inquiry is not strictly whether there was an "actual" reduction to

[1] It is noted for the record that the type of disclosure contained in the Emery et al. patent is not compliant with the requirements of Section 101 or 112 according to the positions set forth in the reports entitled "Comparative study on biotechnology patent practices - Theme: Nucleic acid molecule-related inventions whose function are inferred based on homology search", which was produced in 2000 under the auspices of Trilateral Project B3b:Mutual understanding in search and examination, and the "Comparative study on biotechnology patent practices - Theme: Comparative study on 'reach-through' claims", which was produced in November 2001, also under the auspices of Trilateral Project B3b: Mutual understanding in search and examination.

practice, but is whether the applied reference contains a disclosure which complies with the requirements of Section 112.

Regarding the Examiner's assertions about Emery et al.'s purported teaching of a ligand for the TR4 receptor, Applicants respectfully disagree. In the previous office action, the Examiner referred to some text in Col. 1, lines 31-40, in the Background of the Invention section of the patent, in which Emery et al. refer to a listing of some of the ligands which had been identified in the art as members of the TNF family. In the present office action at page 4, lines 17-19, the Examiner states that while "Emery et al. does not single out Fas Ligand as binding TR4, it does list it among the ligands that bind the receptors of the superfamily to which TR4 belongs." Applicants submit that the mere mention by Emery et al. of a list of TNF family ligands in the Background section of the patent falls significantly short of a teaching, or even a suggestion, that Fas ligand does indeed bind TR4. One skilled in the art reading the entire disclosure of Emery et al. is not taught nor is motivated to believe that TR4 is a receptor for Fas ligand.

Recognizing the unpredictable nature of this field of technology, without any teaching of a function or activity of the receptor or the identity of a ligand that binds the putative receptor, the disclosure of the reference cannot enable one of ordinary skill. Moreover, Applicants respectfully submit that the disclosure of Emery et al. is non-enabling for any claims directed to TR4 DNA, TR4 protein or TR4 antibodies. Those skilled in the art readily understood at the time of the filing of Emery et al. that the TNF receptor family (to which the TR4 receptor belongs) is an extensive family whose members have wide and varied biological activities. The Emery et al. patent admits such at Col. 2, lines 13-15, stating that "[t]he effects of TNF family ligands and TNF family receptors are varied and influence numerous functions, both normal and abnormal...". The varied and unpredictable nature of the TNF family is also evidenced by the many references cited in the enclosed review articles by Locksley et al. and Wallach (and those cited references pre-date the filing of Emery et al.). For

the Examiner's convenience, copies of the Locksley et al. and Wallach review articles are being provided with this submission, along with a Supplemental Information Disclosure Statement.

To further illustrate the deficiencies of the Emery et al. patent, Applicants direct the Examiner's attention to the following points:

- The Emery et al. patent states that TR4 shares the highest degree of homology to TNFR-2, roughly 29%. *See, e.g., Col. 6, lines 45-55.* This is a relatively low percentage of homology between TR4 and TNFR-2. TR4 is a soluble receptor (unlike TNFR-2 which is a membrane-bound receptor) and does not have an intracellular signaling capacity. Accordingly, any inferences, if any, that can be drawn about the activity of TR4 and TNFR-2 based on such homology are not a sufficient basis upon which to reasonably predict activity or function.

- The Emery et al. patent discloses that TR4 is expressed in cDNA libraries of keratinocytes, pancreatic tumor, lung endothelium, prostate, cerebellum, fetal heart, retinal pigment epithelium, and progesterone treated endometrial stromal cells, and in Northern blots of spleen, lung thymus, heart, and a neuroblastoma cell line. *See, e.g., Col. 6, lines 64-67; Col. 16, lines 5-40.* Such expression data is not conclusive and lacks any interpretation of the receptor's function or activity as it shows expression in varied tissues types and in both normal and cancerous tissues.

- The Emery et al. patent suggests that the TR4 polypeptide, and TR4 antibodies, can be used in the treatment of a long and varied list of conditions, from inflammation to cancer to AIDS *(see, e.g., Col. 2, lines 40-47; Col. 11, lines 20-27; Col. 12, lines 25-42)*. No reasoning for this suggestion is given, so apparently Emery et al. was only extrapolating from information known about

the many and varied biological effects of other TNF receptor family members. Such extrapolation is entirely speculative and is not enabling to those skilled in the art. The definition of the activity of TR4 in the Emery et al. patent is likewise confusing and circular:

> 'TR4 activity or TR4 polypeptide activity' or 'biological activity of the TR4 or TR4 polypeptide' refers to the metabolic or physiologic function of said TR4 including similar activities or improved activities or these activities with decreased undesirable side-effects. Also included are antigenic and immunogenic activities of said TR4. *See, Col. 3, lines 1-6.*

Accordingly, for at least the reasons set forth above, Applicants respectfully request the Examiner to withdraw the rejection under 35 U.S.C. § 102(e) in view of Emery et al.

Section 103 Rejections

Claim 84 was rejected under Section 103(a) as being unpatentable over Emery et al. and US Patent 4,946,778. Applicants respectfully traverse this rejection on grounds that Emery et al. cannot properly be cited as prior art against the claims presented in this application, for at least the reasons above. Thus, it is believed this rejection under Section 103 should also be withdrawn.

Respectfully submitted,
GENENTECH, INC.

Date: December 11, 2003 By: Diane L Marschang

Diane L. Marschang
Reg. No. 35,600
Telephone No. (650) 225-5416